PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/007669	08.07.2004	11.07.2003

International Patent Classification (IPC) or both national classification and IPC
A61K9/72, A61K9/14, A61K47/12, A61P11/06

Applicant
GLAXO GROUP LIMITED

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/EP2004/007669

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was field, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The following document has not been furnished:

   ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).

   ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

   Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 18

because:

☒ the said international application, or the said claims Nos. 18 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-10
	No:	Claims	11-19
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-19
Industrial applicability (IA)	Yes:	Claims	1-17,19
	No:	Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Section III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claim 18 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

Re Section V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: WO 01/78694 A
   D2: US-A-5 202 309
   D3: WO 02/078671 A
   D4: WO 00/28979 A

   D1 (see example 12) discloses an inhalable solid formulation comprising salbutamol sulphate, lactose and an additive (e.g. calcium stearate). On page 15 (second paragraph) it is disclosed that the additive includes "those materials which will tend to decrease the cohesion between the active particles and the carrier particles".

   D2 (see example VIII) discloses a method comprising mixing calcium stearate with an active ingredient substance (compound I) and a carrier (lactose).

   D3 (see p. 7, l. 30-32) discloses the use of e.g. calcium stearate and magnesium stearate for improving the stability of active materials in medicinal suspension aerosol formulations using HFA 134a or HFA 227 as propellant (carrier).

D4 (see claims 1, 3, 8 and 17) discloses the use of magnesium stearate for improving the moisture resistance of dry powder formulations for inhalation which contain active material and carrier (e.g. lactose).

2. The subject-matter of independent claims 11 and 17-18 is not novel (Art. 33(2) PCT) over D1 (see above under item 1).

3. The subject-matter of independent claim 19 is not novel (Art. 33(2) PCT) over D1 and D2 (see above under item 1).

4. The subject-matter of independent claims 14 and 15 is not novel (Art. 33(2) PCT) over D1, D2 and D3, said documents disclosing methods comprising mixing calcium stearate with active ingredient and carrier (see above under item 1); see also below under Section VIII.

5. The subject-matter of independent claims 1 and 2 is novel (Art. 33(2) PCT) since the specific use defined therein has not been disclosed in any of the available prior art documents.

6. The subject-matter of claim 1 differs from that of D1 (closest prior art) only in specifying that the calcium stearate inhibits *chemical* interaction, whereas in D1 the calcium stearate inhibits adhesive interaction. However, it is known from D3 (p. 7, l. 24-31) that calcium stearate improves stability of active materials. Furthermore, it is known from D4 (claim 1) that magnesium stearate (which according to D1 and D3 appears to be interchangeable with calcium stearate) improves moisture resistance in dry powder formulations. Hence, there are strong hints in the prior art (D1 in combination with D3 or D4) that calcium stearate will reduce chemical interaction between active ingredient and carrier. Consequently, in the absence of any unexpected effects, the subject-matter of claim 1 is not considered to involve an inventive step (Art. 33(3) PCT).